Remarks

This is supplemental to Applicants' (First) Request for Reconsideration filed June 30, 2006, and incorporates by reference in its entirety the Remarks set forth in Applicants' First Request.

As additional support for applicants' position, a series of experiments were performed to show that the claimed invention is not obvious based on the prior art.

As set forth in Applicants' First Request, there is no suggestion in Sherrington of substituting the gel of Sherrington with the irreversibly bound layering particles (latex) of the present invention. Moreover, the examples of Sherrington disclose grinding HIPE polymers into particulate form (size 250 to 1500 μM) prior to infusion of a gel. There are two isolated suggestions in Sherrington that the substrate to be infused could be a monolith block, but it provides no details regarding how to infuse the gel into a monolith (Claim 1) or how to make this product into a chromatographic separation column capable of reasonable flow rates at acceptable backpressure (Claim 7).

Nonetheless, Dr. Kelly Flook has performed comparative experiments to show that if one attempted to make a gel-infused monolith using the Sherrington gel and monolith, it would not be suitable for use as a flow-through ion exchange medium (Claim 1), particularly a chromatography separation column (Claim 7). A Declaration by Dr. Flook setting forth the details of such experiments will be submitted within one month.

Sherrington discloses preparation of a polyHIPE block which is milled into small pieces. The milled pieces are rotated in a flask with an acrylamide monomer gel in a solution containing swelling solvent (dichloroethane) to infuse the gel into the pores. The gel-infused pieces are washed with dimethylformamide (DMF) and diethyl ether.

There is no disclosure in Sherrington of how to adapt this method to a procedure for making a chromatography monolith using polyHIPE and acrylamide gel of the same type. Dr. Flook used the following procedure in an attempt to do so. The polyHIPE monolith was formed *in situ* in a chromatography column body (dimension 4.6 mm diameter, 50 mm length) and washed to remove unreacted components, as generally disclosed in U.S. Patent 4,522,953, the

procedure referenced in Sherrington, and allowed to dry. Then a syringe pump was filled with solution of acrylamide monomer dissolved in a dichloroethane solvent. The acrylamide solution was pumped from the syringe through the column, and the ends of the column were sealed. Polymerization of the monomer was performed by placing the column in a water bath at 60°C for one hour.

Then, DMF was pumped through the column at a flow rate of 0.1 ml/min to remove unattached gel. When the backpressure exceeded 1000 psi, small pieces of polymer extruded out of the column into a waste beaker. After a short time, the backpressure dropped significantly. On investigation, the column was empty of polymeric material, suggesting that the polyHIPE polymer was not structurally strong enough to withstand swelling and washing.

These results confirm why the polyHIPE material of Sherrington was milled and sieved in the Sherrington examples prior to gel infusion; namely, the polyHIPE material monolith was not suited for high pressure liquid chromatography.

Even though there was no detailed disclosure of a monolith other than the polyHIPE of Sherrington, Applicants substituted for the polyHIPE a monolith column of the type sold by Dionex Corporation under the trademark ProSwift RP-1S (the "Dionex monolith") and infused the same acrylamide gel in the foregoing method. When the backpressure reached the maximum pressure limit of the pump (2000 psi), flow of DMF was stopped. No flow of solution through the gel infused Dionex monolith could be established even when the flow rate was reduced to 0.05 ml/min. Typically this column would be operated for chromatographic applications at a flow rate of 1 ml/min or greater and the linear velocity under these conditions would be calculated as 0.1 cm/sec. (If flow would have been established at the flow rate of 0.05 ml/min this would translate into a linear velocity of 0.005 cm/sec which is too low to be useful for liquid chromatography.)

In contrast, a Dionex monolith (dimension 0.25 mm diameter, 250 mm in length) was filled with latex particles generally according to the method described in the present specification ("the claimed monolith"). At a flow rate of 0.015 ml/min, the back pressure was 900 psi, an acceptable flow rate and backpressure for chromatography. It should also be noted that the backpressure of the uninfused Dionex monolith was substantially unchanged after infusion with

the latex particles. The flow rate of 0.015 ml/min translates into a linear velocity of 0.5 cm/sec. The equivalent flow rate with a 4.6 mm x 50 mm column made by the present invention would be 5 ml/min. In contrast no flow could be established in the gel infused monolith at 0.05 ml/min and at a backpressure of 2000 psi, the upper pressure limit of the pump. In Dr. Flook's opinion, this lack of flow is caused by the gel filling the pores of the monolith through which the solution would otherwise flow.

By way of summary, no flow of solution could be established in a gel-filled monolith column, even one using the Dionex monolith, and even at a backpressure substantially in excess of that used for liquid chromatography. In contrast, a monolith including the irreversibly bound fine ion exchange layering particles of the claims has substantially the same backpressure as the empty monolith, and is perfectly suitable for high pressure liquid chromatography. This clearly establishes the superiority of the claimed invention over the cited prior art. This is true even if there were a motivation in the prior art to use the layering particles instead of the gel, which there is not. Moreover, the experiments show that a gel-filled monolith according to Sherrington was inoperable for use as a liquid chromatography medium.

For the foregoing reasons, it is submitted that the claims are now in condition for allowance.

The Commissioner is authorized to charge fees which may be required, including extension fees, or credit any overpayment, to Deposit Account No. 50-0310 (Ref:).

Please direct any calls in connection with this application to the undersigned at (415) 442-1174.

Respectfully submitted,

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